UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/373,230	08/12/1999	HARUKI OKMURA	OKAMURA=2E	2359

1444 7590 01/05/2004

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 01/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/373,230	OKMURA ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11 and 14-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *7-9* is/are allowed.

6)☒ Claim(s) *1-6, 11 and 14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED OFFICE ACTION

Applicant's amendment filed on 19 August 2003 is acknowledged and entered. Following the amendment, claims 1-3, and 11 are amended, and the new claims 16 and 17 are added.

Currently, claims 1-9, 11, 14-17 are pending and under consideration.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-6 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is indefinite because it is unclear what the new limitation of "a sequence variant of SEQ ID NO:2" is meant, i.e., up or down to what % of sequence identity of SEQ ID NO:2 is still considered such a sequence variant? The metes and bounds of the claim, therefore, cannot be determined. For the same reason, the term "the N-terminal region" is indefinite, i.e., up to what length from the N-terminal is still considered "the N-terminal region"? The claim is further indefinite for the recitation of "*an* amino acid sequence of SEQ ID NO:2" because the term "an" indicates more than one sequence in SEQ ID NO:2, while the fact is that there is only one contiguous sequence of SEQ ID NO:2 disclosed in the specification. "The" is suggested to replace "an". The claim is further indefinite for the recitation of "*physicochemical* property (3)" in the last line of the claim because property (3) is not a physicochemical property, rather, it is a biological property. The claim is further indefinite because it is unclear if the variant must have all properties as recited at the start of the claim, or only the biological activity.

Claim 11 is indefinite because it is unclear what "the same antigenic fragments" are. The claim is further indefinite because it is unclear whether the sequence variant have to retain any property other than "antigenic fragment".

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-6 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to a specific variant of said protein, which has an amino acid sequence of SEQ ID:2 where residue 70 is methionine or threonine, does not reasonably provide enablement for with claims to variants having physicochemical and functional properties listed in parts (1) to (4) of claim 3, and having the amino acid sequence of SEQ ID NO:2 with at least one amino acid residue in SEQ ID:2 replaced with different amino acid, or at least one amino acid residue deleted or added to the N-terminus of SEQ ID:2 while not substantially altering physicochemical properties of the protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims, for the reasons set forth in the previous Office Actions, paper No. 7 and 13, and for the reasons below.

Applicants argument on 19 August 2003 has been fully considered, but is not deemed persuasive for reasons below.

At pages 9-10 of the response, the applicant argues that the variant is a sequence variant of SEQ ID NO:2, that a skilled artisan would understand the upper limit of the number of amino acids being replaced even if there is no explicit limitation recited, which is considered to be several to dozens of amino acids at most, or would have been obvious to one of skill in the art in view of the art, and that if claim 3 is rejected, the variants of SEQ ID NO:2 would not be protected, which would be unfair. This argument is not persuasive because the claim, as written, reads on functional equivalent of the SEQ ID NO:2 as it recites "which is obtainable by replacing at least one amino acid residue in SEQ ID NO:2". As the "*sequence variant* of SEQ ID NO:2" is not defined in the specification, such a limitation is not given patentable weight, thus, without the upper limit of the number of amino acids being replaced, the claim, given the broadest interpretation, encompasses functional variants that may not have sequence similarity to SEQ ID

NO:2 overall, but meet the limitations in parts (1)-(4). Such functional variants are not disclosed in the present specification, and therefore, are not entitled to patent protection as to the present invention. Further, as such a functional variant is never described in the specification, the specification fails to teach how to make a commensurate number of such species, and undue experimentation would be required of the skilled artisan to make the claimed invention in its full scope.

Claims 1, 2, 11, 14 and 15 remain rejected, and the new claims 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to a protein with SEQ ID NO:2, wherein residue 70 is methionine or threonine, does not reasonably provide enablement for any IL-18 (claims 1, 2, 16 and 17, for example) or variants with properties listed in these claims (claims 11, 14 and 15, for example). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims, for the reasons set forth in the previous Office Actions, paper No. 7 and 13.

Applicants argument filed on 19 August 2003 has been fully considered, but is not deemed persuasive for the reasons below.

The newly amended claims 1 and 2 eliminate the sequence requirement for the protein, and the new claim 16 does not have any structural limitation. As such, the claims read on any or all proteins or IL-18 having said physicochemical and functional properties. The present specification of merely discloses two distinct species of the IFN- γ inducing protein with single amino acid substitution, it does not provide clear direction or enough guidance, nor working examples to teach how to make a commensurate number of the claimed species meeting the limitations of the claims. There is no way to predict, for example, the sequence structure of any "IGIF" or "IL-18" other than the two disclosed in the specification, and undue experimentation is required prior to using the claimed invention in its full scope.

With respect to claim 11, Applicants indicates, at page 11 of the response, that the amendment overcomes the enablement rejection of the claim. This is not deemed persuasive for the reasons below. Part (4) of the claim is amended with the limitation of "a sequence variant of

the protein having one or more of the same antigenic fragments as in the amino acid sequence of SEQ ID NO:2". As one antigenic fragment can be a fragment of 4-6 amino acids, which may have no association with the functional property of the protein, such a limitation reads on a functional variant of the protein. Additionally, "a mAb specific to a sequence variant of the protein" encompasses mAbs specific to the non-common sequences comparing to SEQ ID NO:2 even though the variant shares antigenic fragments of SEQ ID NO:2. Further, the specification does not disclose any antigenic fragment specific to SEQ ID NO:2. Therefore, the antibody limitation and the limitation of antigenic fragments do not further specify the sequence structure of the variant, and it reads on a functional variant of the protein. As the specification does not disclose any of such functional equivalents, and of antigenic fragments specific to SEQ ID NO:2, nor the relationship between antigenic fragments and functional property, the specification fails to teach how to make a commensurate number of such species, and undue experimentation would be required of the skilled artisan to make the claimed invention in its full scope.

Claims 1-6, 11, 14 and 15 remain further rejected, and the new claim 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons set forth in the previous Office Actions, paper No. 7 and 13.

Applicants argument filed on 19 August 2003 has been fully considered, but is not deemed persuasive for reasons below.

At page 12 of the response, the applicant argues that the subject matter is well described in the present specification as that "the functional variants which have the amino acid sequence of SEQ ID NO:2, and react with monoclonal antibody specifically reacting with SEQ ID NO:2", and that "the functional variants which have a sequence variant of SEQ ID NO:2 with one or more of the same antigenic fragments as in the amino acid sequence of SEQ ID NO:2, and react with monoclonal antibody specifically reacting with said sequence variant". This argument is not deemed persuasive because the cited description reads on functional variants without defined sequence structure that is obvious to one of skilled in the art as the specification does not disclose any of such functional equivalents, and of antigenic fragments specific to SEQ ID NO:2,

nor the relationship between antigenic fragments or sequence structure and the functional property. As such, a skilled artisan cannot envision the existence of such a functional equivalent of SEQ ID NO:2, and therefore conception is not achieved until reduction to practice has occurred.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, 6, 11, 14 and 15 remain rejected, and the new claim 16 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakamura *et al.* (*Infect. Immun.* 61: 64-70, 1993), for the reasons set forth in the previous Office Actions, paper Nos. 4, 7 and 13.

Applicants argument filed on 19 August 2003 has been fully considered, but is not deemed persuasive for reasons below.

At pages 13 to 14 of the response, the applicant argues that the presently claimed protein and Nakamura's factor are not the same because: Okamura (the reference the Examiner cited to support the rejection) indicates that IGIF in the serum sample was proved to be the same IGIF as found in the liver extract (Nakamura's IGIF), and it was considered to be bound to another protein or to exist in an oligomeric form, and thus it cannot be construed that Okamura concludes that Nakamura's factor is same as IGIF. This argument is not persuasive because Okamura concludes that the two IGIFs are the same, and there is no evidence that physical binding to another protein has changed the sequence structure of Nakamura's IGIF. The existence of merely different physical forms of the same molecule does not render the molecule itself patentably distinct in the absence of evidence to the contrary.

At page 14 of the response, the applicant further argues that the molecular weight of the presently claimed protein is different from Nakamura's factor, and that Nakamura's factor is distinguishable from the claimed protein in its existing form even if Nakamura's factor

comprises IGIF. This argument is not persuasive because different existing forms of the same molecule do not render the molecule itself patentably distinct for the same reasons above.

At pages 15 to 16 of the response, the applicant argues that Nakamura's factor loses IFN-γ inducing activity when treated on SDS-PAGE, whereas the claimed protein retains the same activity after treatment on SDS-PAGE, and otherwise, it would have been impossible to determine the molecular weight of the claimed protein in Experiment 2-1, because a molecular weight measured on a protein which has lost its activity on SDS-PAGE does not reflect the true molecular weight as that possessing the activity. This argument is not persuasive for the following reasons. The specification states, as pointed out by applicants, that the purified protein was electrophoresed in a SDS polyacrylamide *gel* free of reducing agent *to mainly show a single band* with an IFN-γ inducing activity at a position ... . The experiment is gel electrophoresis, which is designed *to show the molecular weight* of proteins, therefore, it is unclear how it is possible that such a experiment can be used for the interpretation of a functional property. The Examiner is not aware that a molecule maintains the same molecular weight on a SDS-PAGE would necessarily retain its functional activity, and that the functional activity can be positively determined solely based on the unchanged molecular weight. Further, as pointed out by the Examiner in the previous Office Action, in the functional assays in Example 2-4 of the present specification, the biological activity of the claimed protein is demonstrated using "a present purified protein". In view of Example 1, which is directed to "preparation of purified protein", "a present purified protein" used in the functional assays demonstrated in Example 2-4 is purified using the procedure in Example 1, not that eluted from SDS-PAGE. Therefore, the "difference" between Nakamura's factor and the protein of the present invention in IFN-γ inducing activity of the protein after treatment on SDS-PAGE is not credible, and cannot be used to support the assertion that the two proteins are distinct.

Conclusion:

Claims 7-9 are allowable.

Advisory Information:

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
12/18/03